

REMARKS

Upon entry of this Amendment, Claims 1 – 6, 9 – 12, 16 – 17, 22 – 27, 32 – 36, 39 – 41, and 46 – 47, and 50 will be pending. Claims 1, 3- 5, 10 – 12, 16 – 17, 22, 24 – 26, 32 – 35, 40 – 41, 46 – 47, and 50 are hereby amended. Claims 13, 14, 30, 31, 42, 43, 44, 45, 48 and 49 are canceled without prejudice to or disclaimer regarding the underlining subject matter. Support for the claim amendments may be found throughout the Specification and claims as originally filed, for example, the Specification at page 6, lines 22 – 27.

Entry and consideration of the remarks and amendments is earnestly solicited.

I. Claim Objections

Applicants thank the Examiner for withdrawing the objections to Claims 16 and 34.

Consistent with the Examiner's suggestion, Applicants have amended Claims 10 – 11 and 40 – 41 by replacing “*ctfA* and *B*” with “*ctfAB*.” As such, Applicants respectfully assert that the claim objections are hereby rendered moot and withdrawal is respectfully requested.

II. Rejection under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 1-6, 9-14, 16-17, 22-27, 30-36, and 39-40 stand rejected under 35 U.S.C. § 112, first paragraph, written description, as allegedly "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Non-Final Office Action at page 4. Applicants respectfully disagree with the Examiner's rejection, but have amended the claims to recite *E. coli* in a manner that is consistent with the Examiner's suggestion in order to facilitate prosecution .

For at least the above reasons, the rejection of the claims over 35 U.S.C. § 112, first paragraph, written description, is rendered moot and withdrawal is respectfully requested.

III. Rejection under 35 U.S.C. § 103(a)

Claims 1-2, 5-6, 9-14, 16, 22-24, 26-27, 30-32, 35-36, 39-46, and 48-50 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,303,352 ("Cameron *et al.*") in view of *Biotechnol. Prog.* 16: pages 940-946 (2000) ("Altaras *et al.*") and further in view of

Appl Environ Microbiol. Mar; 64(3):pages 1079-85 (1998) (“Bermejo *et al.*”). Applicants respectfully disagree, but have amended the claims in order to facilitate prosecution. As such, Applicants respectfully submit that the claim rejections are rendered moot and withdrawal is respectfully requested.

A. Method Claims 1 – 2, 5 – 6, and 9 – 12 are separately patentable

In rejecting the claims, the Examiner asserts that “the phrase ‘causing evolution’ comprises genetic engineering, such as deletion of genes.” Non-Final Office Action at page 11. The Examiner further asserts that “[t]herefore, in combining the above references, one of ordinary skill in the art would have recognized the advantage of further ‘evolving’ the microorganism of Cameron *et al.*.” *Id.* Applicants respectfully disagree.

As amended, Claim 1 clarifies the manner in which the evolution is performed. For example, part “c” of Claim 1 recites “...having an improved 1,2-propanediol synthase activity by applying increasing rates of dilution in such a way as to conserve in the growth medium only those *E.coli* strain that display a growth rate equal to or higher than the imposed rate of dilution to provide an evolved strain.” None of Cameron *et al.*, Altaras *et al.*, or Bermejo *et al.* teach or suggest this methodology.

Additionally, Cameron *et al.* fails to teach any one of steps (b) – (d) of independent Claim 1. Cameron *et al.* describes a method for producing 1,2-propanediol by culturing a recombinant microorganism which expresses recombinant methylglyoxal synthase activity and a recombinant activity of aldose reductase, glycerol dehydrogenase and/or pyridine nucleotide transferase. Cameron *et al.* at page 2, lines 44 – 56. This method is achieved by the transformation of microorganisms with a synthetic operon. As acknowledged by the Examiner, Cameron *et al.* does not teach or suggest further “evolution” of the *E.coli* strain. Non-Final Office Action at page 9.

Neither Altaras *et al.* nor Bermejo *et al.* remedy the deficiencies of Cameron *et al.* and neither reference provides motivation to modify the methodology of Cameron *et al.* in a manner that would render the claims obvious. Altaras *et al.* sets forth different ways to improve

production of R-1,2-propanediol by *E. coli*. For instance, Altaras *et al.* describes construction of strains with inactivation of *IdhA* and/or *gloA* genes by transducing antibiotic resistance markers. Altaras *et al.* at abstract. In another aspect, Altaras *et al.* describes the construction of strains that co-express the genes *mgs* and *gldA* with either *adhl* or *fuc0*. *Id.* In addition to failing to teach or suggest “c” of Claim 1, Altaras *et al.* does not provide motivation to modify the strain of Cameron *et al.* in a manner that would render the claims obvious.

In citing to Bermejo *et al.*, the Examiner provides no motivation as to why one of ordinary skill in the art would simultaneously be motivated to delete of *IdhA* while at the same time increasing expression of a *C. acetobutylicum* gene. Moreover, none of Cameron *et al.*, Altaras *et al.*, or Bermejo *et al.* teach or suggest that the specific deletion of *IdhA* together with increased expression of a *C. acetobutylicum* gene would result in a strain with enhanced 1,2-propanediol, let alone a strain with a decreased acetate concentration. In maintaining the rejections, the Examiner has failed to consider the interrelatedness of three distinct methodologies. With this, one of ordinary skill in the art would have no motivation to combine the teachings Cameron *et al.*, Altaras *et al.*, or Bermejo *et al.* with a reasonable expectation of success.

As such, for at least the reasons above, Cameron *et al.* in view of Altaras *et al.* and Bermejo *et al.* do not render the claims obvious. Accordingly, withdrawal of the rejections is respectfully requested.

B. Evolved Strain Claims 16, 22 – 24, 32, 35 – 36, 39 – 41, 46, and 50 are separately patentable

For at least the reasons described above, Claims 16, 22 – 24, 32, 35 – 36, 39 – 41, 46, and 50 reciting an evolved strain are separately patentable and Cameron *et al.* in view of Altaras *et al.* and Bermejo *et al.*, alone or in combination, do not render the claims obvious. Accordingly, withdrawal of the rejections is respectfully requested.

IV. Claims 3 – 4, 17, 25, 33 – 34, and 47

Applicants respectfully submit that at least Claims 3 – 4, 17, 25, 33 – 34, and 47 are in

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condition for allowance. Applicants note that Claims 3 – 4, 17, 25, 33 – 34, and 47 were not rejected by the Examiner as being obvious over Cameron *et al.* in view of Altaras *et al.* and Bermejo *et al.* Applicants also note that the 35 U.S.C. § 112, first paragraph, written description, rejection has been rendered moot by way of the present amendment and Response.

CONCLUSION

In view of the amendments and remarks above, Applicants respectfully submit that this application is in condition for allowance and request favorable action thereon. The Examiner is invited to contact the undersigned at (202) 508-3400 if any additional information is required.

Respectfully submitted,

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